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30aug02 13:29:12 User208669 Session D2097.1
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File 155:MEDLINE(R) 1966-2002/Aug W4
*File 155: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.

Set Items Description
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09949408 98374322 PMID: 9707617
Efficient expression of CFTR function with adeno-associated virus vectors that carry shortened CFTR genes.
Zhang L; Wang D; Fischer H; Fan P D; Widdicombe J H; Kan Y W; Dong J Y
Gene Therapy Core Center for Cystic Fibrosis and Genetic Diseases and Department of Laboratory Medicine, University of California, San Francisco, CA 94143, USA.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Aug 18 1998, 95 (17) p10158-63, ISSN 0027-8424 Journal Code: 7505876
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Adeno-associated virus (AAV)-based vectors have been shown to be effective in transferring the cystic fibrosis gene (CFTR) into airway epithelial cells in animal models and in patients. However, the level of CFTR gene expression has been low because the vector cannot accommodate the CFTR gene together with a promoter. In this study, we described a strategy to reduce the size of the CFTR cDNA to allow the incorporation of an effective promoter with the CFTR gene into AAV vectors. We engineered and tested 20 CFTR mini-genes containing deletions that were targeted to regions that may contain nonessential sequences. Functional analyses showed that four of the shortened CFTRs (one with combined deletions) retained the function and the characteristics of a wild-type CFTR, as measured by open probability, time voltage dependence, and regulation by cAMP. By using an AAV vector with a P5 promoter, we transduced these short forms of CFTR genes into target cells and demonstrated high levels of CFTR expression. We also demonstrated that smaller AAV/CFTR vectors with a P5 promoter expressed the CFTR gene more efficiently than larger vectors or a vector in which CFTR gene was expressed from the AAV inverted terminal repeat sequence. The CFTR mini-gene with combined deletions was packaged into AAV virions more efficiently, generated higher titers of transducing virions, and more effectively transferred CFTR function into target cells. These new vectors should circumvent the limitations of AAV vector for CFTR expression. Our strategy also may be applicable to other genes, the sizes of which exceed the packaging limit of an AAV vector.
Record Date Created: 19980917
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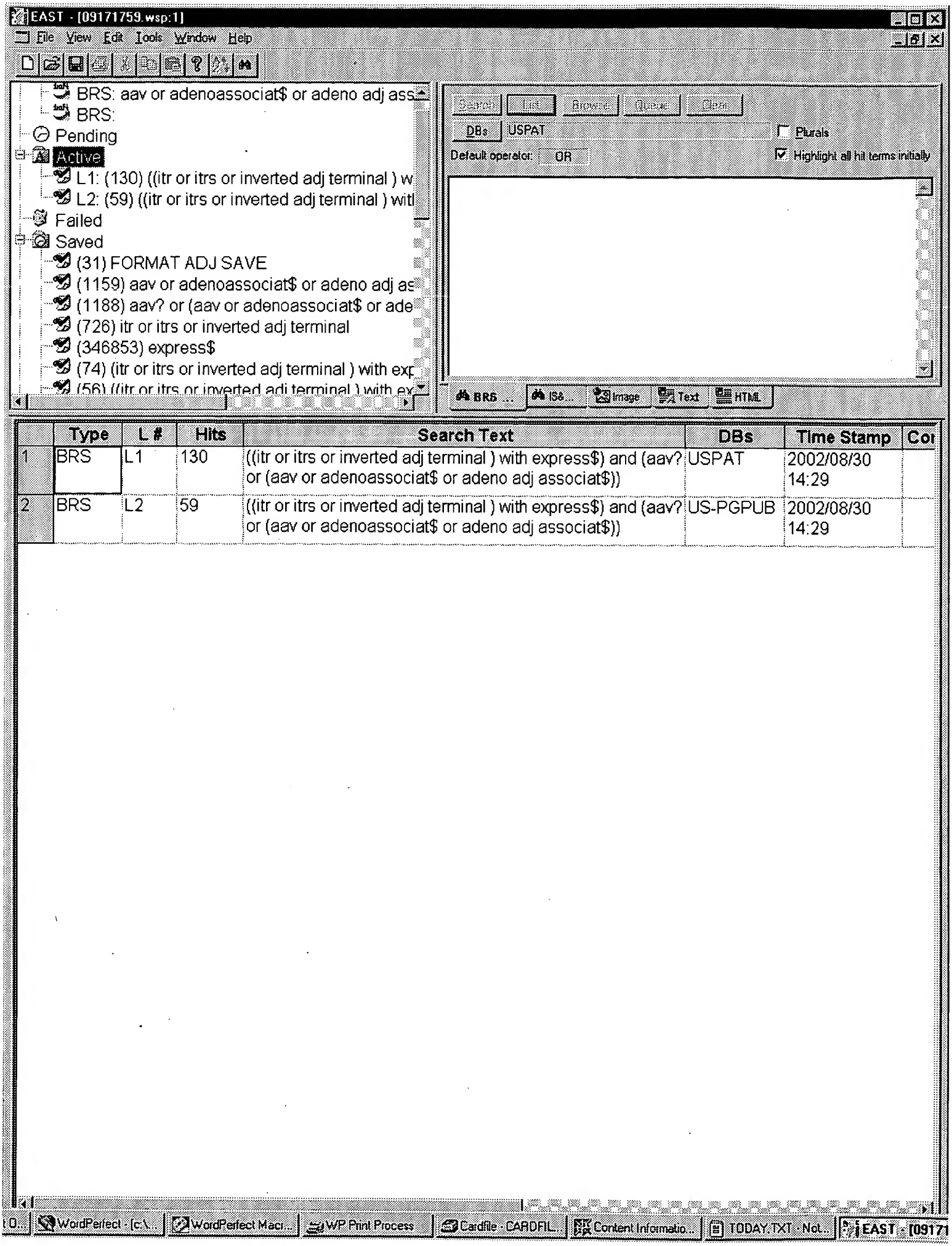
Logoff: level 02.08.23 D 13:30:29



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2	BRS	L2	59	((itr or itrs or inverted adj terminal) with express$) and (aav? or (aav or adenoassociat$ or adeno adj associat$))	US-PGPUB	2002/08/30 14:29	